CERTIFICATE OF MAILING
37 C.F.R. § 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:

July 12, 2007
Date

Sharon V. Hart
Sharon V. Hart

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Philip E. Thorpe and Sophia Ran (As Amended)

Serial No.: 10/621,269

Filed: July 15, 2003

For: Selected Antibody Compositions for Binding to Aminophospholipids (As Amended)

Group Art Unit: 1642

Examiner: Goddard, L.

Atty. Dkt. No.: 4001.003000

THIRD DECLARATION OF
PHILIP E. THORPE UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, PHILIP E. THORPE, HEREBY DECLARE AS FOLLOWS:

1. I am a co-inventor of the subject matter disclosed and claimed in the captioned patent application.

2. I am Professor of Pharmacology and hold the Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology at the Simmons Comprehensive Cancer Center, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, U.S.A. A copy of my *Curriculum Vitae* is attached as **Exhibit A**.

3. I have reviewed the captioned patent application again. I understand the claims in the captioned patent application to be drawn to purified antibodies, or antigen-binding fragments thereof, which bind to phosphatidylserine (PS), preferably in an ELISA recited in the claims, and have the characteristics as defined in the claims; and to compositions comprising, hybridomas producing and methods for preparing such antibodies.

4. I have reviewed the second Official Action issued by the U.S. Patent and Trademark Office (P.T.O.), the agency charged with assessing the patentability of the captioned patent application. I have also reviewed the documents cited in the second Official Action, including Rote *et al.*, *Clin. Immunol. Immunopathol.*, 66:193-200, 1993 (Rote *et al.*, 1993) and published PCT patent application WO 00/02584, of which I am a co-inventor.

5. I understand that, in the second Official Action, the P.T.O. has taken the position that most claims of the captioned patent application lack novelty over Rote *et al.*, 1993 or WO 00/02584. One particular question that the P.T.O. has raised is whether the antibody termed 3SB9b (now known simply as 3SB), as reported in Rote *et al.*, 1993 and WO 00/02584, effectively competes with the 3G4 antibody for binding to PS, such as determined using an ELISA as recited in the claims of the captioned patent application.

6. I am providing the present Declaration and providing the attached evidence to demonstrate that the 3SB antibody does not effectively compete with the 3G4 antibody for binding to PS in an ELISA as recited in the claims of the captioned patent application.

7. Evidence of the fact that 3SB does not effectively compete with 3G4 for binding to PS in such an ELISA is presented in **Exhibit B**, which shows the results of an ELISA competition study using the 3SB and 3G4 antibodies.

8. The data of **Exhibit B** were generated from a competitive binding ELISA, in accordance with those described in the captioned patent application. In order to detect bound 3G4 antibody, as distinct from any 3SB, a chimeric form of the 3G4 antibody (ch3G4) was used in which the mouse variable regions are linked to human IgG constant regions. Chimeric 3G4 binds to PS in the same manner as murine 3G4, by virtue of the mouse variable regions, but can be detected and differentiated from the 3SB antibody (mouse IgM) by using a detection agent specific for the human constant regions. The competitive assay was conducted as follows. The ELISA plate was coated with PS and blocked with 10% FBS. ch3G4 was kept constant at 6.67 nM, and titrated down with 3SB, starting at 100 nM. Bound ch3G4 was detected with goat anti-human IgG-HRP. An isotype-matched mouse IgM antibody of irrelevant specificity (GV39M) was used as a control for 3SB.

9. As shown in **Exhibit B**, the addition of increasing amounts of the 3SB antibody does not result in any detectable reduction in binding of the ch3G4 antibody to PS (ch3G4 binding remains essentially constant at 100% in the presence of increasing amounts of 3SB, very similar to the results using the control antibody). This demonstrates that 3SB does not effectively compete with 3G4 for binding to PS.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the captioned patent application or any patent issued thereon.

July 9, 2007
Date

Philip E. Thorpe
Philip E. Thorpe, Ph.D.

EXHIBIT A

Curriculum Vitae - EXHIBIT A

Name:	Philip Edward THORPE
Place of Birth:	Smethwick, Worcestershire, U.K.
Nationality:	British (with U.S. Permanent Residency)
Home Address:	5510 Morningside Drive Dallas, TX 75206
Social Security #:	452-99-7852

EDUCATION:

1962-1969	Moseley Grammar School, Birmingham B17, U.K.
1969-1972	University of Liverpool, U.K.
Academic Qualifications:	First Class B.Sc (Hons) Degree in Pharmacology (Summa cum Laude)

Postgraduate Education:

1972-1975	Medical Research Council Scholarship Division of Surgical Sciences Clinical Research Centre London, U.K. Ph.D. supervisors: Sir Peter Medawer, Dr. Stella Knight

POSTDOCTORAL EMPLOYMENT:

1975-1981	Medical Research Council Fellow Division of Biology Chester Beatty Research Institute Institute of Cancer Research Royal Cancer Hospital Fulham Road Chelsea London SW3 6JB, U.K.
1981 - 1991	Director, Drug Targeting Laboratory Imperial Cancer Research Fund Lincoln's Inn Fields London WC2A 3PX, U.K.
1991 - 1998	Professor of Pharmacology Serena Simmons Distinguished Chair in Cancer Immunopharmacology

Department of Pharmacology and
Hamon Center for Therapeutic Oncology Research
University of Texas Southwestern Medical Center
5323 Harry Hines Boulevard
Dallas, Texas 75235-8593

1998 - 1999

Director of Oncology Research
Associate Director of the Center for Molecular Medicine
Maine Medical Center Research Institute
125 John Roberts Road, Suite #5
South Portland, Maine 04106

1999 – present

Professor of Pharmacology
Serena Simmons Distinguished Chair in Cancer Immunopharmacology
Simmons Comprehensive Cancer Center and Hamon Center for
Therapeutic Oncology Research
University of Texas Southwestern Medical School
NC7.340
2201 Inwood Rd.
Dallas, TX 75235-8794

Telephone: 214 648-1268 or 214 648-1499
Fax: 214 648-1613
philip.thorpe@utsouthwestern.edu

UT SOUTHWESTERN GRADUATE PROGRAM APPOINTMENTS:

Cell Regulation Graduate Program, UTSW
Immunology Graduate Program, UTSW

GRADUATE SCHOOL TEACHING (annual):

Mechanisms of Drug Action Course (Director)
Medical Pharmacology Course
Human Biology and Disease Course
Cancer Biology Course
Physician's Assistant Course

UT SOUTHWESTERN COMMITTEES

Promotion and Tenure Committee, 1997-98
Graduate Admissions Committee, 1994-96
Clinical Research Scientific Review And Monitoring Committee, 1997-8
Department of Cell and Molecular Biology Review Committee, 1997-8
Radioactive Drug Research Committee, 2003-present
American Cancer Society Institutional Review Group, 2004-present

PROFESSIONAL SOCIETIES:

American Association for Cancer Research
American Association for Immunology
American Society for Pharmacology and Experimental Therapeutics
North American Vascular Biology Organization
Sigma Xi
Society for Biological Therapy

SCIENTIFIC ADVISORY BOARDS:

Scientific Advisory Board, Cytopharm Inc., Munich, Germany, 1990-1996
Scientific Advisory Board, Texcellon Inc., Dallas, TX, 1990-1993
Scientific Advisory Board, Peregrine Pharmaceuticals, Inc., Princeton, NJ, 1993-1997
Scientific Advisory Board, Repair, Inc., Portland, ME, 1998-2000
Scientific Advisory Board, Peregrine Pharmaceuticals, Inc., Tustin, CA, 1997-present
Scientific Advisory Board, Arcus Therapeutics, Inc., Boston, MA, 2000-2002
Founding Scientist, Peregrine Pharmaceuticals, Inc., Tustin, CA

EDITORIAL BOARDS:

IRCS Journal of International Research Communication, 1974-1984
Advanced Drug Delivery Research Reviews, 1985-1992
Antibody, Immunoconjugates and Radiopharmaceuticals, 1987-1995
Bioconjugate Chemistry, 1989-present
Journal of Drug Targeting, 1992-2000
Therapeutic Immunology, 1992-present
Angiogenesis, 1997-present
Cancer Biotherapy and Radiopharmaceuticals, 2004-present

INTERNATIONAL CONFERENCES ORGANIZED:

Co-organizer (with Dr. G. Gregoriadis), NATO meeting on Receptor Mediated Targeting of Drugs, Greece,1983
Vice Chairman, Gordon Research Conference on Drug Carriers in Medicine and Biology, Ventura, CA 1996
Chairman (with Dr. Ruth Duncan), Gordon Research Conference on Drug Carriers in Medicine and Biology, Ventura, CA, 1998
Chairman, 1st International Symposium on Vascular Targeting, Boston, MA, 2002
Chairman, 2nd International Symposium on Vascular Targeting, Miami, FL, 2004

INVESTIGATIONAL NEW DRUG (IND) APPLICATIONS

RFB4-SMPT-dgA for Treatment of B-lymphoma (with Dr. E. Vitetta), 1989
RFT5-SMPT-dgA for Treatment of Hodgkin's Disease (with Dr. E. Vitetta), 1992
Tarvacin™ for Treatment for Hepatitis C virus (with Peregrine Pharmaceuticals, Inc.), 2005

HONORS AND AWARDS:

Pierce Immunotoxin Award, 1988
The State of Texas House of Representatives Resolution recognizing his contribution to cancer research, 1997.
American Cancer Society 'Award of Excellence', 1999

GRANTS (since 1991):

Past

Vascular Targeting: A New Approach to the Therapy of Solid Tumors; Dallas Biomedical Corporation; $161,832 direct for the period of October 1, 1991-December 31, 1992.

Heparin-Steroid Conjugates: A New Class of Angiogenesis Inhibitors for Clinical Applications: Dallas Biomedical Corporation; $134,613 direct for the period of October 1, 1991 to December 31, 1992.

Vascular Targeting: A New Approach to the Therapy of Solid Tumors; Elsa U. Pardee Foundation; $64,843 for the period of May 1, 1992-April 30, 1993.

Vascular Targeting Program; Dallas Biomedical Corporation; $119,123 direct for the period of January 1, 1993-June 30, 1993.

Recombinant Antibodies for Targeting the Vasculature of Solid Tumors; Elsa U. Pardee Foundation; $128,658 direct for the period of June 1, 1993-May 31, 1995.

New Angiogenesis Inhibitors for the Therapy of Breast Cancer; American Cancer Society DHP-95; $150,000 direct for the period of July 1, 1993-June 30, 1995.

Developmental project funded from Dr. John Minna's SPORE Grant 1 P50 CA709097 from the National Institutes of Health; $20,000 direct for the period of September 1, 1996-August 30, 1997.

Holder of the Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology, annual income $60,000.

Vascular Targeting: A New Approach to the Therapy of Solid Tumors and Rheumatoid Arthritis; Anonymous Donor; $1,666,665 direct for the period of September 1, 1992-December 31, 1997.

Mechanisms of drug action and disposition; National Institutes of Health T32-GM07062 (training grant, PI-Dr. Alfred Gilman); $54,000 direct for the period of September 1, 1994-August 31, 1999.

Vascular Targeting Agents that Home to and Destroy or Coagulate Tumor Vasculature; Peregrine Pharmaceuticals; $480,000 for the period of December 1, 1994-December 1, 1997.

Vascular Targeting Agents for Infarcting Lung Cancer; Advanced Research Program from the State of Texas; $247,500 direct for the period of January 1, 1996-December 31, 1997.

Therapeutic Clotting to Destroy Solid Tumors; Advanced Technology Program from the State of Texas; $190,579 for the period of January 1, 1998-December 31, 1999.

Angiogenesis Inhibitors for Therapy of Solid Tumors; National Institutes of Health 5-RO1-CA59569; $781,718 direct for the period of December 15, 1993-November 30, 1999.

Collateral Tumor Targeting; Sponsored Research Agreement with Techniclone Corporation; $1,050,000 direct for the period of April 1999-March 2001

Immunotoxins for the Treatment of Hodgkin's Disease; National Institutes of Health 5-RO1-CA54168; $820,052 direct for the period of April 1, 1991-May 31, 2000.

Targeting the Vasculature of Solid Tumors; National Institutes of Health 1-RO1-CA74951; $728,529 direct for the period of December 1, 1997-November 30, 2001.

Specific coagulation of tumor vasculature. Texas Technology ARP grant; $200,000

Present

Novel anti-viral agents for treating Lassa fever. NIH, $1,798,285, 2003-08.

Naked antibodies for treating cancer; Sponsored Research Agreement with Peregrine Pharmaceuticals, Inc., $500,000 per year direct (since 1999)

Therapeutic clotting to destroy solid tumors; Gillson Longenbaugh Foundation, Houston, Texas; $50,000 per year

Anti-angiogenic drugs for childhood brain cancer. Chesler Foundation, $10,000 per year.

VEGF-rGel for targeting the vasculature of breast cancer (M.Rosenblum, P.I). Dept. of Defense. $43,000 per year for 2002-5.

Simmons Foundation, Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology, $86,000 per year.

Vascular Targeting Antibodies for Improving Chemotherapy of Prostate Cancer (P. Thorpe, PI). Department of Defense; $210,000 per year

Synergy between anti-phosphatidylserine monoclonal antibody, 3G4 and docetaxel for treatment of breast cancer (X. Huang, PI; P. Thorpe, Co-PI), Susan Komen Foundation for Basic, Clinical and Translational Breast Cancer Research; $200,000 per year

A strategy for enhancing the effect of radiation in the treatment of breast cancer (T. Luster, Fellowship). American Cancer Society; $80,000 per year

PATENTS

Issued

1. Heterobifunctional linking agents derived from N-succinimido-dithio-alpha methyl-methylene-benzoates (Inventor: P. Thorpe)
   U.S. Patent No. 4,880,935

2. Purification of A-chain immunotoxins (Inventor: P. Thorpe)
   U.K. Patent No. 43606 P3474

3. Methods and compositions for the treatment of Hodgkin's disease (Inventors: P. Thorpe and A. Engert)
   U.S. Patent No. 5,165,923

4. Preparation and use of steroid-polyanionic polymer-based conjugates targeted to vascular endothelial cells (Inventor: P. Thorpe)
   U.S. Patent No. 5,474,765
   U.S. Patent No. 5,762,918

5. Methods and compositions for targeting the vasculature of solid tumors (Inventors: P. Thorpe and F. Burrows)
   U.S. Patent No. 6,004,554
   U.S. Patent No. 5,965,132
   U.S. Patent No. 5,855,866
   U.S. Patent No. 5,776,427
   U.S. Patent No. 5,863,538
   U.S. Patent No. 6,051,230
   U.S. Patent No. 6,261,535
   European Patent No. 0 627 940 (17 countries, including France, Germany, U.K.)

6. Antibodies that bind to endoglin (Inventors: P. Thorpe and F. Burrows)
   U.S. Patent No. 5,660,827

7. VEGF-Gelonin for targeting the vasculature of solid tumors (Inventor: P. Thorpe)
   U.S. Patent No. 6,451,312

8. Methods and compositions for the coagulation of tumor vasculature (Inventors: P. Thorpe and T. Edgington)
   U.S. Patent No. 6,093,399
   U.S. Patent No. 6,004,555
   U.S. Patent No. 5,877,289
   U.S. Patent No. 6,036,955
   U.S. Patent No. 6,749,853
   European Patent No. 0 771 216 (16 countries, including France, Germany, U.K.)
   Australian Patent No. 702250
   New Zealand Patent No. 288883
   Hungarian Patent No. 220347
   Singapore Patent No. 35823
   Mexican Patent No. 212,225

9. Tissue Factor methods, compositions and combination for coagulation and tumor treatment (Inventors: P. Thorpe, S. King and B. Gao)
    U.S. Patent No. 6,156,321
    U.S. Patent No. 6,132,729
    U.S. Patent No. 6,132,730
    European Patent No. 0 988 056 (15 countries, including France, Germany, U.K.)
    Australian Patent No. 735187
    New Zealand Patent No. 336720
    Singapore Patent No. 66589

10. Cancer treatment methods using antibodies to aminophospholipids (Inventors: P. Thorpe, S. Ran)
    U.S. Patent No. 6,406,693
    Australian Patent No. 771224
    New Zealand Patent No. 508950

11. Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids (Inventors: P. Thorpe, S. Ran, R. Brekken)
    U.S. Patent No. 6,312,694
    European Patent No. 1 098 665 (15 countries, including France, Germany, U.K.)
    Australian Patent No. 750414
    Singapore Patent No. 78111
    New Zealand Patent No. 508873

12. Antibody and antibody conjugate compositions and kits for selectively inhibiting VEGF (Inventors: P. Thorpe, R. Brekken)
    U.S. Patent No. 6,342,219
    U.S. Patent No. 6,342,221
    U.S. Patent No. 6,416,758
    U.S. Patent No. 6,524,583
    U.S. Patent No. 6,676,941
    U.S. Patent No. 6,703,020
    Australian Patent No. 774287
    Australian Patent No. 763954
    European Patent No. 1 179 541
    South African Patent No. 2001/8612
    South African Patent No. 2001/8285

Pending

44 pending regular U.S. patent applications and 186 pending international patent applications directed to compositions and methods for the diagnosis and treatment of cancer and viral infections

PUBLICATIONS:(Total = 173 plus 1 submitted)

1. Thorpe, P. E. and Knight, S. C. (1974) Microplate culture of mouse lymph node cells. I. Quantitation of responses to allogeneic lymphocytes and phytomitogens. J. Immunol. Methods **5**: 387-404.

2. Thorpe P. E., Knight, S. C. and Farrant, J. (1976) Optimal conditions for the preservation of mouse lymph node cells in liquid nitrogen using cooling rate techniques. Cryobiology **13**: 126-138.

3. Thorpe, P. E., Ross, W. C. J., Cumber, A. J., Hinson, C. A., Edwards, D. C. and Davies, A. J. S. (1978) Toxicity of diphtheria toxin for lymphoblastoid cells is increased by conjugation to anti-lymphocytic globulin. Nature **271**: 752-754.

4. Ross, W. C. J., Thorpe, P. E., Cumber, A. J., Edwards, D. C., Hinson, C. A., and Davies, A. J. S. (1980) Increased toxicity of diphtheria toxin for human lymphoblastoid cells following covalent linkage to anti-(human lymphocyte) globulin or its $F(ab^1)_2$ fragment. Eur. J. Biochem. **104**: 381-390.

5. Davies, A. J. S., Edwards, D. C. and Thorpe, P. E. (1981) Introduction to a symposium on new trends in human immunology and cancer immunotherapy. In 'New Trends in Human Immunology and Cancer Immunotherapy'. pp 1-7.

6. Thorpe, P. E., Cumber, A. J., Williams, N., Edwards, D. C., Ross, W. C. J. and Davies, A. J. S. (1981) Abrogation of the non-specific toxicity of abrin conjugated to anti-lymphocyte globulin. Clin. Exp. Immunol. **43**: 195-200.

7. Thorpe, P. E., Brown, A. N. F., Ross, W. C. J., Cumber, A. J., Detre, S. I., Edwards, D. C., Davies, A. J. S. and Stirpe, F. (1981) Cytotoxicity acquired by conjugation of an anti-Thy 1.1 monoclonal antibody and the ribosome-inactivating protein, gelonin. Eur. J. Biochem. **116**: 447-454.

8. Edwards, D. C. and Thorpe, P. E. (1981) Targeting toxins - the retiarian approach to chemotherapy. Trends in Biochemical Sciences, 313-316.

9. Edwards, D. C., Smith, A., Ross, W. C. J., Cumber, A. J., Thorpe, P. E. and Davies, A. J. S. (1981) The effect of abrin, anti-lymphocyte globulin and their conjugates on the immune response of mice to sheep red blood cells. Experientia **37**: 256-257.

10. Skilleter, D. N., Paine, A. J. and Thorpe, P. E. (1981) Selective direction or ricin to hepatic parenchymal cells. Biochem. Soc. Transactions **10**: 122-123.

11. Thorpe, P. E., Cumber, A. J., Davies, A. J. S., Edwards, D. C., Ross, W. C. J. and Smith, A. (1982) The immunosuppressive effects of anti-Thy 1.1 $F(ab^1)_2$ conjugated to abrin. In 'Antibodies as Carriers of Anticancer Drugs or Toxins: Quo Vadis?' (F. K. Jansen and R. Roncucci, eds.) SANOFI, Montpellier, France, pp. 134-135.

12. Thorpe, P. E., Brown, A., Cumber, A. J., Davies, A. J. S., Edwards, D. C., Ross, W. C. J. and Stirpe, F. (1982) Selective cytotoxicity with a conjugate of anti-Thy 1.1 antibody and gelonin.

In 'Antibodies as Carriers of Anticancer Drugs or Toxins: Quo Vadis?' (F. K. Jansen and R. Roncucci, eds.) SANOFI, Montpellier, France, pp. 123-124.

13. Edwards, D. C., Ross, W. C. J., Cumber, A. J., McIntosh, D., Smith, A., Thorpe, P. E., Brown, A., Williams, R. H. and Davies, A. J. S. (1982) A comparison of the in vitro and in vivo activities of conjugates of anti-mouse lymphocyte globulin and abrin. Biochim. Biophys. Acta **71**: 272-277.

14. Edwards, D. C., Thorpe, P. E. and Davies, A. J. S. (1982) Antibody-toxin conjugates as potential therapeutic agents. In 'Targeting of Drugs' (G. Gregoriadis, J. Senior, and A. Trouet, eds.) Plenum Press, N. Y. and London, pp. 83-96.

15. Thorpe, P. E., Ross, W. C. J. (1982) The preparation and cytotoxic properties of antibody-toxin conjugates. Immunol. Rev. **62**: 119-158.

16. Thorpe, P. E., Edwards, D. C., Davies, A. J. S., Ross, W. C. J. (1982) Monoclonal antibody-toxin conjugates: aiming the magic bullet. In 'Monoclonal Antibodies in Clinical Medicine' (A. McMichael and J. Fabre, eds.) Acad. Press, London, pp. 167-201.

17. Thorpe, P. E., Mason, D. W., Brown, A. N. F., Simmonds, S. J., Ross, W. C. J., Cumber, A. J. and Forrester, J. A. (1982) Selective killing of malignant cells in a leukaemic rat bone marrow using an antibody-ricin conjugate. Nature **297**: 594-596.

18. Mason, D. W., Thorpe, P. E., Ross, W. C. J. (1982) Elimination of leukaemic cells from rodent bone marrow in vitro with antibody-ricin conjugates: implications for autologous marrow transplantation in man. Cancer Surveys **1**: 389-415.

19. Davies, A. J. S., Jansen, F. K., Olsnes, S., Thorpe, P. E., Wofsy, L. and Edwards, D. C. (1982) Antibodies as toxin carriers in cancer immunotherapy. In 'Current Chemotherapy and Immunotherapy' (Proceedings of the 12th Int. Congress of Chemotherapy, Vol. **2**) (Periti, P. and Grassi, G. G. Eds.) pp. 1141-1143.

20. Thorpe, P. E., Brown, A., Foxwell, B. and Myers, C. (1983) Blockade of the galactose-binding site of ricin by its linkage to antibody. In 'Monoclonal Antibodies and Cancer' (B. D. Boss, R. Langman, I. Trowbridge and R. Dulbecco, eds.) Acad. Press (London) Ltd., pp. 117-124.

21. Vodinelich, L., Myers., C., Sutherland, R., Thorpe, P. E. and Greaves, M. F. (1983) WT1: a monoclonal antibody in T-cell acute lymphoblastic leukemia. Leukemia Reviews International **1**, 263.

22. Thorpe, P. E., Detre, S. I., Mason, D. W., Cumber, A. J. and Ross, W. C. J. (1983) Monoclonal antibody therapy: 'model' experiments with toxin conjugated antibodies in mice and rats. Haematology and Blood Transfusion **28**: 107-111.

23. Rennie, D. P., McGregor, A. M., Wright, J., Weetman, A. P., Hall, R. and Thorpe, P. E. (1983) An immunotoxin of ricin A chain conjugated to thyroglobulin selectively suppresses the antithyroglobulin autoantibody response. Lancet **ii**, 1338-1340.

24. Thorpe, P. E., Ross, W. C. J., Brown, A. N. F., Myers, C. D., Cumber, A. J., Foxwell, B. M. J. and Forrester, J. A. (1984) Blockade of the galactose-binding sites of ricin by its linkage to

antibody: specific cytotoxic effects of the conjugates. Eur. J. Biochem. **140**: 63-71.

25. Sikora, K., Smedley, H. and Thorpe, P. E. (1984) Tumor Imaging and Drug Targeting. Brit. Med. Bull. **40**: 233-239.

26. Myers, C. D., Thorpe, P. E., Ross, W. C. J., Cumber, A. J., Katz, F. E., Tax, W., and Greaves, M. F. (1984) An immunotoxin with therapeutic potential in T cell leukemia: WT1-ricin A. Blood **63**: 1178-1185.

27. Foxwell, B. M. J., Ross, W. C. J. and Thorpe, P. E. (1984) Antibody-ricin conjugates: a method of linkage which blocks the galactose binding site of ricin. Behring Inst. Mitt., **74**: 101-107.

28. Thorpe, P. E. (1984) Antibody-toxin conjugates as anti-cancer agents. In 'Cancer Chemotherapy and Selective Drug Development' (Harrap, K. R., Davies, W. and Calvert, A. H. eds.) Martinus-Nijhoff Publishing Co., Boston, The Hague, Dordrecht and Lancaster, pp. 263-267.

29. Paraskeva, C., Buckle, B. G. and Thorpe, P. E. (1985) Selective killing of contaminating human fibroblasts in epithelial cultures derived from colorectal tumours using an anti-Thy-1 antibody-ricin conjugate. Br. J. Cancer **51**: 131-134.

30. Foxwell, B. M. J., Detre, S. I., Donovan, T. A. and Thorpe, P. E. (1985) The use of anti-ricin antibodies to protect mice intoxicated with ricin. Toxicology **34**: 79-88.

31. Cumber, A. J., Forrester, J. A., Foxwell, B. M. J., Ross, W. C. J. and Thorpe, P. E. (1985) The preparation of antibody-toxin conjugates. Methods in Enzymology **112**: 207-224.

32. Thorpe, P. E., Detre, S. I., Foxwell, B. M. J., Brown, A. N. F., Skilleter, D. N., Wilson, G., Forrester J. A. and Stirpe, F. (1985) Modification of the carbohydrate in ricin with metaperiodate-cyanoborohydride mixtures: effects on toxicity and in vivo distribution. Eur. J. Biochem. **147**: 197-206.

33. McIntosh, D. and Thorpe, P. (1985) Role of the B-chain in the cytotoxic action of antibody-ricin and antibody-abrin conjugates. In 'Receptor-Mediated Targeting of Drugs' (Gregoriadis, G., Poste, G., Senior, J. and Trouet, A. eds.) NATO ASI Series A, **82**: 105-118.

34. Foxwell, B. M. J., Donovan, T. A., Thorpe, P. E. and Wilson, G. (1985) The removal of carbohydrates from ricin with endoglycosidases H, F, and D and ∀-mannosidase. Biochim. Biophys. Acta **840**: 193-203.

35. Lord, J. M., Roberts, L. M., Thorpe, P. E. and Vitetta, E. S. (1985) Immunotoxins. Trends in Biotechnology **3**: 175-180.

36. Thorpe, P. E., Brown, A. N. F., Bremner, J. A. G., Foxwell, B. M. J. and Stirpe, F. (1985) An immunotoxin composed of monoclonal anti-Thy 1.1 antibody and a ribosome-inactivating protein from Saponaria officinalis: Potent antitumor effects in vitro and in vivo. J. Natl. Cancer Inst. (USA) **75**: 151-159.

37. Vitetta, E. S. and Thorpe, P. E. (1985) Immunotoxins containing ricin A or B chains with

modified carbohydrate residues act synergistically in killing neoplastic B cells in vitro. Cancer Drug Delivery **2**: 191-198.

38. Thorpe, P. E. (1985) Antibody Carriers of Cytotoxic Agents in Cancer Therapy: A Review. In 'Monoclonal Antibodies '84: Biological and Clinical Applications'. (A. Pinchera, G. Doria, F. Dammacco and A. Bargellesi, eds.) Editrice Kurtis s.r.l., Milan, Italy. pp. 475-512.

39. Skilleter, D. N., Price, R. J., Thorpe, P. E. (1985) Modification of the carbohydrate in ricin with metaperiodate and cyanoborohydride mixtures: effect on binding, uptake and toxicity to parenchymal and non-parenchymal cells of rat liver. Biochim. Biophys. Acta **842**: 12-21.

40. Skilleter, D. N., Price, R. J., Thorpe, P. E. and Foxwell, B. M. J. (1985) Mannose oligosaccharides in ricin are involved in the selective uptake of the toxin by hepatic non-parenchymal cells. Human Toxicology **5**: 126, 1986.

41. Wawrzynczak, E. and Thorpe, P. E. (1986) Monoclonal Antibodies and Therapy. In 'Introduction to the Cellular and Molecular Biology of Cancer' (L. M. Franks and N. M. Teich, eds.) Oxford University Press, (Oxford, N. Y. & Tokyo) pp. 378-410.

42. Blakey, D. C. and Thorpe, P. E. (1986) Immunotoxins. BioEssays **4**: 292-297.

43. Fulton, R. J., Blakey, D. C., Knowles, P. P., Uhr, J. W., Thorpe, P. E., Vitetta, E. S. (1986) Purification of ricin A_1, A_2 and B-chains and characterization of their toxicity. J. Biol. Chem. **261**: 5314-5319.

44. Blakey, D. C. and Thorpe, P. E. (1986) Effect of chemical deglycosylation on the in vivo fate of ricin A-chain. Cancer Drug Delivery **3**: 189-196.

45. Wawrzynczak, E. J. and Thorpe, P. E. (1986) Complete enzymic deglycosylation of ricin B-chain. FEBS Letters **207**: 213-216.

46. Foxwell, B. M. J., Blakey, D. C., Brown, A. N. F., Donovan, T. A. and Thorpe, P. E. (1987) The preparation of deglycosylated ricin by recombination of glycosidase-treated A and B-chain: effects of deglycosylation on toxicity and in vivo distribution. Biochim. Biophys. Acta **923**: 59-65.

47. Thorpe, P. E. and Mason, D. W. (1987) Monoclonal antibody-toxin conjugates: theory, experimental approaches and early clinical results in marrow transplantation in man. In 'Tumour Markers' (A. S. Daar, ed.) Blackwell Scientific Publ. Ltd., (London) pp. 178-203.

48. Vitetta, E. S. and Thorpe, P. E. (1987) Immunotoxins. In 'New avenues in Developmental Cancer Chemotherapy' (Proceedings of the 8th Annual Bristol-Myers Symposium on Cancer Research'. (K. Harrap and T. A. Connors, eds.) Academic Press, N. Y. and London. pp. 265-276.

49. Knowles, P. P. and Thorpe, P. E. (1987) Purification of immunotoxins containing ricin A-chain and abrin A-chain using Blue Sepharose CL-6B. Anal. Biochem. **160**: 440-443.

50. Blakey, D. C., Watson, G. J., Knowles, P. P., and Thorpe, P. E. (1987) Effect of chemical

deglycosylation of ricin A-chain on the in vivo fate and cytotoxic activity of an immunotoxin composed of ricin A-chain and anti-Thy 1.1 antibody. Cancer Res. **47**: 947-952.

51. Blakey, D. C., Wawrzynczak, E. J., Stirpe, F. and Thorpe, P. E. (1987) Anti-tumour activity of a panel of anti-Thy 1.1 immunotoxins made with different ribosome inactivating proteins. In 'Membrane-Mediated Cytotoxicity'. UCLA Symposia on Molecular and Cellular Biology, Volume **45** (B. Bonavida and R. J. Collier, eds.) Alan R. Liss, Inc., pp. 195-202.

52. Wawrzynczak, E. J., Falasca, A., Jeffery, W. A., Watson, G. M. and Thorpe, P. E. (1987) Identification of a tyrosine residue in the saccharide binding site of ricin B-chain using N-[^{14}C]-acetylimidazole. FEBS Letters **219**: 51-55.

53. O'Hare, M., Roberts, L. M., Thorpe, P. E., Watson, G. J. Prior, B. and Lord, J. M. (1987) Expression of ricin A chain in Escherichia coli. FEBS Letters, **216**: 73-78.

54. Stirpe, F., Derenzini, M., Barbieri, L., Farabegoli, F., Brown, A. N. F., Knowles, P. P., Thorpe, P. E. (1987) Hepatotoxicity of immunotoxins made from saporin, a ribosome-inactivating protein from Saponaria officinalis. Virchows Arch. B Cell Path **53**: 259-271.

55. Glennie, M. J., McBride, H. M., Worth, A. T., Stirpe, F., Thorpe, P. E. and Stevenson, G. T. (1987) Emergence of immunoglobulin variants following treatment of a B-cell leukemia with an immunotoxin composed of anti-idiotypic antibody and saporin. J. Exp. Med. **166**: 43-62.

56. Wawrzynczak, E. and Thorpe, P. E. (1987) Methods for preparing immunotoxins: effect of the linkage on activity and stability. In 'Immunotoxins: current methods and approaches for the targeting of toxins and other substances.' (Vogel, C. W., ed.) Oxford University Press, pp. 28-55.

57. Thorpe, P. E., Wallace, P. M., Knowles, P. P., Relf, M. G., Brown, A. N. F., Watson, G. J., Knyba, R. E. Wawrzynczak, E. J. and Blakey, D. C. (1987) New coupling agents for the synthesis of immunotoxins containing a hindered disulfide bond with improved stability in vivo. Cancer Res. **47**: 5924-5931.

58. Katz, F. E., Janossy, G., Cumber, A., Ross, W., Blacklock, H. A., Tax, W. and Thorpe, P. E. (1987) Elimination of T cells from human peripheral blood and bone marrow using a cocktail of three anti-T cell immunotoxins. Br. J. Haematol. **67**: 407-411.

59. Thorpe, P. E., Blakey, D. C., Brown, A. N. F., Knowles, P. P., Knyba, R. E., Wallace, P. M., Watson, G. J. and Wawrzynczak, E. (1987) Comparison of two anti-Thy 1.1-abrin A-chain immunotoxins prepared with different crosslinking agents: antitumor effects, in vivo fate and tumor cell mutants. J. Natl. Cancer Inst. **79**: 1101-1112.

60. Barnett, M.J., Rohatiner, A.Z., Kingston, J.E., Adams, K.E., Batten, E.L., Bassen, R., Thorpe, P.E., Horton, M.A., Malpas, J.S. and Lister, T.A. (1987) In vitro treatment of bone marrow from patients with T-cell acute lymphoblastic leukemia and non-Hodgkin's lymphoma using the immunotoxin WT1-ricin A. Hematologie Und Bluttransfusion **31**: 57-58.

61. Blakey, D.C. and Thorpe, P. E. (1988) An overview of therapy with immunotoxins containing ricin or its A-chain. ANTIBODY, Immunoconjugates and Radiopharmaceuticals, **1**: 1-16.

62. Blakey, D. C., Skilleter, D. N., Price, R. J. and Thorpe P. E. (1988) Uptake of native and deglycosylated ricin A-chain immunotoxins by mouse liver parenchymal and non-parenchymal cells in vitro and in vivo. Biochim. Biophys. Acta **968**: 172-178.

63. Till, M., May, R. D., Uhr, J. W., Thorpe, P. E. and Vitetta, E. S. (1988) An assay that predicts the ability of monoclonal antibodies to form potent ricin A chain-containing immunotoxins. Cancer Res. **48**: 1119-1123.

64. Blakey, D.C., Watson, G. J., Knowles, P. P. and Thorpe, P.E. (1988) The effect of chemical deglycosylation of ricin A-chain on the therapeutic potential of ricin A-chain immunotoxins. In 'Proceedings of International Symposium on Lectins and Glycoconjugates in Oncology'. Springer-Verlag Press, pp. 97-102.

65. Ghetie, M., May, R. D., Till, M., Uhr, J. W., Ghetie, V., Knowles, P. P., Relf, M., Brown, A. N., Wallace, P. M., Janossy, G., Amlot, P., Vitetta, E. S. and Thorpe, P. E. (1988) Evaluation of ricin A chain-containing immunotoxins directed against CD19 and CD22 antigens on normal and malignant human B cells as potential reagents for in vivo therapy. Cancer Res. **48**: 2610-2617.

66. Foxwell, B. M. J., Band, H. A., Long, J., Jeffery, W. A., Snook, D., Thorpe, P. E., Watson, G., Parker, P., Epenetos, A. A. and Creighton, A. M. (1988) Conjugation of monoclonal antibodies to a synthetic peptide substrate for protein kinase: a method for the labelling of antibodies with ^{32}P. Br. J. Cancer **57**: 489-493.

67. Blakey, D. C. and Thorpe, P. E. (1988) The prevention of carbohydrate-mediated clearance of ricin-containing immunotoxins by the liver. In 'Immunotoxins'. (A.E. Frankel, ed.) Martinus Nijhoff Publ., Boston pp. 457-473.

68. Wawrzynczak, E. J. and Thorpe, P. E. (1988) Effect of chemical linkage upon the stability and cytotoxic activity of A-chain immunotoxins. In 'Immunotoxins' (A. E. Frankel, ed.) Martinus Nijhoff Publ., Boston pp. 239-251.

69. Drobniewski, F. A., Thorpe, P. E., Wallace, P. M. and Wawrzynczak, E. J. (1988) The potential of membrane-acting toxins for targeted cancer therapy. In 'Targeting of Drugs: Anatomical & Physiological Considerations' (G. Gregoriadis & G. Poste eds.) Plenum Press, N. Y. & London, pp. 103-108.

70. Blakey, D. C., Wawrzynczak, E. J., Wallace, P. M. and Thorpe, P. E. (1988) Antibody-toxin conjugates: a perspective. Progress in Allergy: Monoclonal antibodies **45**: 50-90.

71. Stirpe, F., Wawrzynczak, E. J., Brown, A. N. F., Knyba, R. E., Watson, G. J., Barbieri, L. and Thorpe, P. E. (1988) Selective cytotoxic activity of immunotoxins composed of a monoclonal anti-Thy 1.1 antibody and the ribosome-inactivating proteins, bryodin and momordin. Brit. J. Cancer **58**: 558-561.

72. Wawrzynczak, E. J., Drake, A. F., Watson, G. J., Thorpe, P. E. and Vitetta, E. S. (1988) Ricin B chain-containing immunotoxins prepared with heat-denatured B chain lacking galactose-binding ability potentiate the cytotoxicity of a cell-reactive ricin A-chain immunotoxin. Biochim. Biophys. Acta **971**: 55-62.

73. Wawrzynczak, E. J., Drake, A. F. and Thorpe, P. E. (1988) Circular dichroism of isolated ricin A- and B-chains. J. Biophys. Chem. **31**: 301-305.

74. Blakey, D. C., Skilleter, D. N., Price, R. J. and Thorpe, P. E. (1988) Comparison of the pharmacokinetics and hepatotoxic effects of saporin and ricin A-chain immunotoxins. Cancer Res. **48**: 7072-7078.

75. Thorpe, P. E., Wallace, P. M., Knowles, P. P., Relf, M. G., Brown, A. N., Watson, G. J., Blakey, D. C. and Newell, D. R. (1988) Improved antitumor effects of immunotoxins prepared with deglycosylated ricin A-chain and hindered disulfide linkages. Cancer Res. **48**: 6396-6403.

76. Shen, G. L., Li, J. L., Ghetie, M. A., Ghetie, V., May, R. D., Till, M., Brown, A. N., Relf, M., Knowles, P., Uhr, J. W., Janossy, G., Amlot, P., Vitetta, E. S. and Thorpe, P. E. (1988) Evaluation of four CD22 antibodies as ricin A chain-containing immunotoxins for the in vivo therapy of human B cell leukemias and lymphomas. Int. J. Cancer **42**: 792-797.

77. Blakey, D. C. and Thorpe, P. E. (1988) Treatment of malignant disease and rheumatoid arthritis using ricin A-chain immunotoxins. Scand. J. Rheumatol. Suppl. **76**: 279-287.

78. Thorpe, P. E. and Blakey, D. C. (1989) Antitumor effects of immunotoxins containing ricin or its A-chain. In 'Clinical Use of Monoclonal Antibodies' (Koene, R. A. P. and Tax, W. J. M., eds.) Actua Sandoz **14**: 92-104.

79. Press, O. W., Martin, P. J., Thorpe, P. E. and Vitetta, E. S. (1988) Ricin A-chain containing immunotoxins directed against different epitopes on the CD2 molecule differ in their ability to kill normal and neoplastic T cells. J. Immunol. **141**: 4410-4417.

80. Li, J. L., Shen, G. L., Ghetie, M. A., May, R. D., Till, M., Ghetie, V., Uhr, J., Janossy, G., Thorpe, P. E., Amlot, P. and Vitetta, E. S. (1989) The epitope specificity and tissue reactivity of four murine monoclonal anti-CD22 antibodies. Cell. Immunol. **118**: 85-99.

81. Blakey, D. C. and Thorpe, P. E. (1989) Anti-tumour effects of monoclonal antibody-ricin conjugates in vitro and in vivo. In 'Clinical Applications of Monoclonal Antibodies' (R. Hubbard and V. Marks, eds.) Plenum Press pp. 233-244.

82. Wiley, R. G., Stirpe, F., Thorpe, P. E. and Oeltmann, T. N. (1989) Neuronotoxic effects of monoclonal anti-Thy 1 antibody (OX7) coupled to the ribosome inactivating protein, saporin, as studied by suicide transport experiments in the rat. Brain Research **505**: 44-54.

83. Engert, A., Burrows, F., Jung, W., Tazzari, P-L., Stein, H., Pfreundschuch, M., Diehl, V. and Thorpe, P. E. (1990) Evaluation of ricin A-chain-containing immunotoxins directed against the CD30 antigen as potential reagents for the treatment of Hodgkin's disease. Cancer Res. **50**: 84-88.

84. Engert, A., Martin, G., Pfreundschuh, M., Diehl, V. and Thorpe, P. E. (1990) Comparison of antitumour effects of ricin A-chain IgG and Fab' immunotoxins for the treatment of Hodgkin's disease. In 'Trends in Drug Research' (V. Claassen, Ed.) Pharmacochemistry Library **13**, pp. 351-361. Elsevier, Amsterdam.

85. Engert, A., Pfreundschuh, M., Diehl, V. and Thorpe, P. E. Development of ricin A-chain immunotoxins for the treatment of Hodgkin's disease and Ki-1 lymphoma. In 'Recent Advances in Chemotherapy' (D. Adam & E. Rubinstein, eds.) Proc. 16th Int. Congr. Chemother., Jerusalem, 1989, pp. 8891-8892.

86. Engert, A., Martin, G., Pfreundschuh, M., Amlot, P., Hsu, S-M., Diehl, V. and Thorpe, P. E. (1990) Antitumor effects of ricin A-chain immunotoxins prepared from intact antibodies and Fab' fragments on solid human Hodgkin's disease tumors in mice. Cancer Res. **50**: 84-88.

87. Wawrzynczak, E. J. and Thorpe, P. E. (1991) Monoclonal Antibodies and Therapy. In 'Introduction to the Cellular and Molecular Biology of Cancer' Second Edition. (L. M. Franks and N. M. Teich, eds.) Oxford University Press (Oxford, N.Y. and Tokyo) pp. 468-509.

88. Engert, A. and Thorpe, P. E. (1990) Antitumor effects of six ricin A-chain immunotoxins of potential use in the treatment of Hodgkin's disease. In 'Targeting of Drugs: Optimization strategies' (G. Gregoriadis, Ed.) Plenum Press, N. Y. & London, pp. 39-48.

89. Engert, A., Thorpe, P. (1990) Immunotoxine: von der Idee der "magic bullet" bis zur klinischen anwendung. Med. Klinik **85**: 555-560.

90. Wawrzynczak, E. J., Watson, G. J., Cumber, A. J., Henry, R. V., Parnell, G. D., Reiber, E. P. and Thorpe, P. E. (1991) Blocked and non-blocked immunotoxins against the CD4 antigen exhibit higher cytotoxic potency than a ricin A-chain immunotoxin potentiated with ricin B-chain or with a ricin B-chain immunotoxin. Cancer Immunol. Immunother **32**: 289-295.

91. O'Hare, M.., Brown, A. N., Hussain, K., Gebhardt, A., Watson, G., Roberts, L. M., Vitetta, E. S., Thorpe, P. E. and Lord, M. (1990) Cytotoxicity of a recombinant ricin-A-chain fusion protein containing a proteolytically-cleavable spacer sequence. FEBS **274**: 200-204.

92. Vitetta, E. S. and Thorpe, P. E. (1991) Immunotoxins. In 'Biologic Therapy of Cancer: Principles and Practice'. (DeVita V., Hellman, S., Rosenberg, S. Eds.). J. B. Lippincott Co. pp. 482-495.

93. Burrows, F. J., Haskard, D. O., Hart, I. R., Poole, S., Thorpe, P. E. (1991) Influence of tumor-derived IL-1 on melanoma-endothelial cell interactions in vitro. Cancer Res. **51**: 4768-4775.

94. Engert, A., Martin, G., Amlot, P., Wijdenes, J., Diehl, V. and Thorpe, P. (1991) Immunotoxins constructed with CD25 monoclonal antibodies and deglycosylated ricin A-chain have potent antitumor effects against human Hodgkin cells in vitro and solid Hodgkin tumors in mice. Int. J. Cancer **49**: 450-456.

95. Vitetta, E. S., Uhr, J. W., Stone, M., Fay, J., May, R., Till, M., Amlot. P., Newman, J., Cunningham, D., Clark, P., Ghetie, V. and Thorpe, P. E. (1991) A Phase I immunotoxin trial in patients with B cell lymphoma. Cancer Res. **51**: 4052-4058.

96. Vitetta, E. S. and Thorpe, P. E. (1991) Immunotoxins containing ricin or its A-chain. Seminars in Cell Biology. **2**: 47-58.

97. Ghetie V., Thorpe, P., Ghetie, M-A., Knowles, P., Uhr, J. W. and Vitetta, E. S. (1991) The GLP large scale preparation of immunotoxins containing deglycosylated ricin A-chain and a hindered disulfide bond. J. Immunol. Meth. **142**: 223-230.

98. Engert, A., Brown, A. and Thorpe, P. (1991) Resistance of myeloid leukemia cell lines to ricin A-chain immunotoxins. Leukemia Res. **15**: 1079-1086.

99. Thorpe, P.E., Wallace, P.M., Knyba, R.E., Watson, G.J., Mahadevan, V.A., Land, H., Yerganian, G., and Brown, P.J. (1991) Selective killing of proliferating vascular endothelial cells by an anti-fibronectin receptor immunotoxin. Int. J. Radiat. Biol. **60**: 24.

100. Lord, J.M., Roberts, L.M. and Thorpe, P.E. (1992) Chimeric proteins containing ricin A chain. In 'Genetically Engineered Toxins'. (A.E. Frankel, Ed). Marcel-Dekker, N.Y., pp. 183-190.

101. Engert, A., Brown, A., Diehl, V. and Thorpe, P. (1992) Screening of 19 monoclonal antibodies for their potential as ricin A-chain immunotoxins against myeloid leukemia cell lines. Haematology and Blood Transfus. **34**: 373-376.

102. Burrows, F. J., Watanabe, Y., and Thorpe, P. E. (1992) A murine model for antibody-directed targeting of vascular endothelial cells in solid tumors. Cancer Res. **52**: 5954-5962.

103. Engert, A. and Thorpe, P. E. (1992) The development of ricin A-chain immunotoxins for clinical trials in patients with Hodgkin's disease. In 'Targeting of Drugs 3: The Challenge of Peptides & Proteins' (G. Gregoriadis, A.T. Florence and G. Poste, eds.) Plenum Press, London, pp. 9-17.

104. Engert, A., Gottstein, C., Winkler, U., Schon, G., Amlot, P., Thorpe, P. and Diehl, V. (1992) New perspectives in oncology: Is selective destruction of tumor cells with immunotoxins in Hodgkin's disease an additional therapeutic alternative? Med. Klin. **87**: 503-509.

105. Vitetta, E. S., Uhr, J. W. and Thorpe, P. E. (1993) Immunotoxin therapy. In 'Cancer: Principles & Practice of Oncology' (V. DeVita, S. Hellman, S. Rosenberg) J.P. Lippincott Publ. Co., Philadelphia, pp. 2624-2636.

106. Thorpe, P. E., Derbyshire, E., Andrade, S. P., Press, N., Knowles, P. P., King, S., Watson, G.J and Rao-Bette, M. (1993) Heparin-cortisol conjugates: New angiogenesis inhibitors with anti-tumor activity in mice. Cancer Res. **53**: 3000-3007.

107. Vitetta, E. S., Thorpe, P. E., Uhr, J. (1993) Immunotoxins: magic bullets or misguided missiles. Trends in Pharmacological Sciences. **14**: 148-154 and Immunology Today **14**: 252-259, 1993 (joint issue).

108. Burrows, F.J. and Thorpe, P.E. (1993) Eradication of large solid tumours in mice with an immunotoxin directed against tumour vasculature. Proc. Natl. Acad. Sci. USA **90**: 8996-9000.

109. Drobniewski, F.A., Watson, G.J., Wawrzynczak, E.J., Alouf, J.E. and Thorpe, P.E. (1993) A novel membrane-acting immunotoxin, the immunolysin, with therapeutic potential. Biochem. Soc. Trans. **20**: 318S.

110. Amlot, P.L., Stone, M.J., Cunningham, D., Fay, J., Newman, J., Collins, R., May, R., McCarthy, M., Richardson, J., Ghetie, V., Ramilo, O., Thorpe, P.E., Uhr, J.W., and Vitetta, E.S. (1993) A phase I study of an anti-CD22-deglycosylated ricin A chain immunotoxin in the treatment of B cell lymphomas resistant to conventional therapy. Blood **82**: 2624-2633.

111. Winkler, U., Gottstein, C., Schön, G., Kapp, U., Wolf, J., Hansmann, M-L., Bohlen, H., Thorpe, P., Diehl, V. and Engert, A. (1994) Successful treatment of disseminated human Hodgkin's disease in SCID mice with deglycosylated ricin A-chain immunotoxins. Blood **83**: 466-475.

112. Burrows, F. J. and Thorpe, P. E. (1994) Targeting the vasculature of solid tumors. J. Controlled Release **28**: 195-202..

113. Burrows, F.J., Overholser, J.P. and Thorpe, P.E. (1994) Potent antitumor effects of an anti-turnor endothelial cell immunotoxin in a murine vascular targeting model. Cell. Biophysics **24/25**: 15-25.

114. Burrows, F.J. and Thorpe, P.E. (1994) Vascular Targeting - a new approach to the therapy of solid tumors. Pharmacology and Therapeutics **64**: 155-174.

115. Engert, A., Gottstein, C., Diehl, V. and Thorpe, P. (1994) Experimental treatment of human Hodgkin's disease with ricin A-chain immunotoxins. Leukemia and Lymphoma **13**: 441-448.

116. Thorpe, P.E. and Burrows, F.B. (1995) Vascular targeting as a new approach to the therapy of solid tumors: validation in a mouse tumor model. In 'Trends and Future Perspectives in Peptide and Protein Drug Delivery' (V.H.L. Lee, M. Hashida, Y. Mizushima) Harwood Academic Publ., Switzerland, pp. 241-251.

117. Thorpe, P.E. (1995) Antibody-directed targeting of the vasculature of solid tumors. American Society of Clinical Oncology Educational Book, pp. 374-377.

118. Derbyshire, E.J., Burrows, F.J., King, S., and Thorpe, P.E. (1995) Immunotoxins for targeting the vasculature of solid tumors. In 'Proceedings of the 7th European Conference on Bacterial Toxins', Copenhagen, June 1995.

119. Thorpe, P.E. and Burrows, F.J. (1995) Antibody-directed targeting of the vasculature of solid tumors. Breast Cancer Res. and Treat. **36**(2): 237-251.

120. Derbyshire, E.J., Comin, G.A., Yang, Y-C., Overholser, J., Watkins, L. and Thorpe, P.E. (1995) Anti-tumor and anti-angiogenic effects in mice of heparin conjugated to angiostatic steroids. Int. J. Cancer **63**:694-701.

121. Burrows, F. J., Tazzari, P-L., Amlot, P., Gazdar, A. F., Derbyshire, E. J., King, S. W., Vitetta, E. S. and Thorpe, P. E. (1995) Up-regulation of endoglin on vascular endothelial cells in human solid tumors: Implications for diagnosis and therapy. Clinical Cancer Res. **1**: 1623-1634.

122. Derbyshire, E.J., Yang, Y-C., Li, S., Comin, G.A., Belloir, J. and Thorpe, P.E. (1996) Heparin-steroid conjugates lacking glucocorticoid or mineralocorticoid activities inhibit the proliferation of vascular endothelial cells. Biochim. Biophys. Acta **1310**: 86-96.

123. Thorpe, P.E. and Burrows, F.B. (1996) Reply to the letter of Griffioen et al. on endoglin/CD105 as a tumor endothelial treatment target. Breast Cancer Res. and Treat. **39**: 241-242.

124. Huang, X., Molema, G., King, S., Watkins, L., Edgington, T.S. and Thorpe, P.E. (1997) Tumor infarction in mice by antibody-directed targeting of tissue factor to tumor vasculature. Science **275**: 547-550.

125. Maier, J.A.M., Delia, D., Thorpe, P.E. and Gasparini, G. (1997) *In vitro* inhibition of endothelial cell growth by the anti-angiogenic drug AGM-1470 (TNP-470) and the anti-endoglin antibody TEC-11. Anti-Cancer Drugs **8**: 238-244.

126. Thorpe, P.E., Wawrzynczak, E.J. and Burrows, F.J. (1997) Monoclonal Antibodies and Therapy. In "Introduction to the Cellular and Molecular Biology of Cancer", Third Edition (L.M. Franks and N.M. Teich, Eds.) Oxford Univ. Press (Oxford, N.Y. and Tokyo) pp. 352-379.

127. Derbyshire, E.J. and Thorpe, P.E. (1997) Targeting the tumour endothelium using specific antibodies. In "Tumour Angiogenesis (R. Bicknell, C. Lewis and N. Ferrara Eds.) Oxford Univ. Press (Oxford, N.Y. and Tokyo) pp. 343-356.

128. Derbyshire, E.J., Gottstein, C. and Thorpe, P.E. (1997) Immunotoxins In "Immunochemistry: A Practical Approach Series", (A.P. Johnstone and M.W. Turner, Eds.) Oxford Unv. Press (Oxford, N.Y. and Tokyo) pp. 239-273.

129. Derbyshire, E.J. and Thorpe, P.E. (1997) Targeting the vasculature of solid tumours. J. Controlled Release **48/2-3**: 277-288.

130. Brekken, R.A., King, S.W., and Thorpe, P.E. (1998) Vascular endothelial growth factor as a marker of tumor endothelium. Cancer Res. **58**: 1952-1959.

131. Ran, S., Gao, B., Duffy, S., Watkins, L., Rote, N. and Thorpe, P.E. (1998) Infarction of solid Hodgkin tumors in mice by antibody-directed targeting of tissue factor to tumor vasculature. Cancer Research, **58**: 4646-53.

132. Gao, B., Li, S., and Thorpe, P.E. (1998) A simple and rapid method for purifying the extracellular domain of human tissue factor. Thromb. Res., **91**(5): 249-53.

133. Huang, X., Gottstein, C., Brekken, R.A. and Thorpe, P.E. (1998) Expression of soluble VEGF receptor 2 and characterization of its binding to VEGF by surface plasmon resonance. Biochem. Biophys. Res. Commun., **252**(3): 643-8.

134. Thorpe, P.E. and Ran, S. (2000) Tumor infarction by targeting tissue factor to tumor vasculature. Cancer J., **6**(suppl. 3): S237-S244.

135. Giatromanolaki, A., Koukourakis, M.J., Sivridis, E., O'Byrne, K., Cox, G., Thorpe, P.E., Brekken, R.A., Gatter, K.C., Harris, A.L. (2000) Co-expression of MUC1 glycoprotein with multiple angiogenic factors in non-small cell lung cancer suggests co-activation of angiogenic and migration pathways. Clin. Cancer Res., **6**:1917-1921.

136. Koukourakis, M.I., Giatromanolaki, A., Thorpe, P.E., Brekken, R.A., Sivridis, E., Kakolyris, S.,

Georgoulias, V., Gatter, K.C., Harris, A.L. (2000) VEGF/KDR activated microvessel density vs. CD31 standard microvessel density in non-small cell lung cancer. Cancer Res., **60**:3088-3095.

137. Feng, D., Nagy, J.A., Brekken, R.A., Pettersson, A., Manseau, E.J., Pyne, K., Mulligan, R., Brekken, R., Thorpe, P.E., Dvorak, H.F., & Dvorak, A.M. (2000) Ultrastructural localization of the Vascular Permeability Factor/Vascular Endothelial Growth Factor (VPF/VEGF) Receptor-2 (FLK-1, KDR) in normal mouse kidney and in hyperpermeable vessels induced by VPF/VEGF-secreting tumors and adenoviral vectors. J. Histochem. Cytochem., **48**:545-555.

138. Brekken, R.A., Overholser, J.P., Stasny, V.A., Waltenberger, J., Minna, J.D., and Thorpe, P.E. (2000) Selective inhibition of VEGFR2 activity by a monoclonal anti-VEGF antibody blocks tumor growth in mice. Cancer Res., **60**, 5117-24.

139. Bergers, G., Brekken, R., McMahon, G., Vu, T.H., Itoh, T., Tamaki, K., Tanzawa, K., Thorpe, P., Itohara, S., Werb, Z., Hanahan, D. McMahon, G. (2000) Matrix metalloproteinase-9 triggers the angiogenic switch during carcinogenesis. Nature Cell Biol., **2**, 737-744.

140. Thorpe, P.E., Ran, S. 2000. Vascular targeting. In "Tumor Angiogenesis and Microcirculation", Eds., Voest, E.E., D'Amore, P.A., Marcel Dekker, Inc., NY pp 549-578.

141. Gottstein, C., Wels, W., Ober, B., and Thorpe, P.E. (2001). Generation and characterization of recombinant Vascular Targeting Agents from hybridoma cell lines. Biotechniques **30**, 190-199.

142. Giatromanolaki, A., Koukourakis, M.I., Sivridis, E, Thorpe, P.E., Brekken, R.A., Konstantinos, S., Fountizilas, G., Gatter K.C., and Harris, A.L. (2000). Tumor specific activation of the VEGF/KDR angiogenic pathway in a subset of locally advanced squamous cell head and neck carcinomas. Clin. & Exp. Metastasis **18**, 313-319.

143. Giatromanolaki, A., Sivridis, E., Athanassou, N., Zois, E., Thorpe, P.E., Brekken, R.A., Gatter, K.C., Harris, A.L., Koukourakis, I.M., and Koukourakis, M.I. (2001). The angiogenic pathway 'vasular endothelial growth factor/flk-1 (KDR)-receptor in rheumatoid arthritis and osteoarthritis. J.Pathol., **194**, 101 - 108.

144. Giatromanolaki, A., Sivridus, E., Brekken, R., Thorpe, P.E., Anastasiadis, P., Gatter, K. C., Harris, A.L., Koukourakis, M. Prognostic and therapeutic implications of VEGF/flk-1 (KDR) angiogenic pathway in endometrical carcinoma. Cancer 92, 2569-2577 (2001)

145. Brekken, R.A. and Thorpe, P.E. (2001). VEGF-VEGF receptor complexes as markers of tumor vascular endothelium. J. Controlled Release **74**, 173 - 181.

146. Guo, P., Xu, L., Yang, S.-T., Pan, S., Brekken, R., Whitaker, G.B., Nagane, M., Thorpe, P., Rosenbaum, J., Huang, H.-J. S., Cavenee, W.K., Cheng, S.-Y. (2001). Vascular endothelial growth factor isoforms display distinct activities in promoting tumor angiogenesis at different anatomic sites. Cancer Res. **61**, 8569-8577.

147. Veenendaal, L.M., Jin, H., Ran, S., Cheung, L., Navone, N., Marks, J.W., Thorpe, P.E., Waltenberger, J. and Rosenblum, M.G. (2002). *In vitro* and *in vivo* studies of a $VEGF_{121}$/rGelonin chimeric fusion toxin targeting the neovasculature of solid tumors. Proc. Nat'l. Acad. Sci. USA, **99:** 7866-7871

148. Ran, S., Downes, A., Thorpe, P.E. (2002). Increased exposure of anionic phospholipids on the surface of tumor blood vessels. Cancer Res. **62**, 6132-40.

149. Thorpe, P.E., and Ran, S. (2002). Mapping zip codes in tumor vasculature. Nature Pharmacogenetics **2**, 205-6.

150. Ran, S., Rote, N., and Thorpe, P E. (2002). Phosphatidylserine is a marker of tumor vasculature and a potential target for anti-cancer drugs. Int. J. Rad. Onc. Res. **54**, 1479-84.

151. Ran, S., Rosenblum, M., and Thorpe, P.E. (2002) Ligand-directed destruction of tumor vasculature. In 'Biomedical Aspects of Drug Targeting' (Eds. V.R. Muzykantov and V.P. Torchilin). Kluwer Acad. Publ. Boston, pp 229-248.

152. Zhang, W., Ran, S., Huang, X., Thorpe, P.E. (2002) A monoclonal antibody that blocks VEGF binding to VEGFR2 (KDR/Flk-1) inhibits tumor growth in an orthotopic human breast cancer model . Angiogenesis 5, 35-44.

153. Mason, R.P., Ran, S., and Thorpe, P.E. (2002) Quantitative assessment of tumor oxygen dynamics: molecular imaging for prognostic radiology. J. Cell Biochem. 87, S39, 45-53.

154. Brantley, D.M., Cheng, N., Thompson, E.J., Lin, Q., Brekken, R.A., Thorpe, P.E., Muraoka, R.S., Cerretti, D.P., Pozzi, A., Jackson, D., Lin, C., Chen, J. (2002) Soluble Eph A receptors inhibit tumor angiogenesis and progression in vivo.
Oncogene 21(46):7011-26.

155. Thorpe, P.E., Chaplin, D.J. and Blakey, D.C. (2003) The First International Conference on Vasculature Targeting: Meeting Overview. Cancer Res. 63, 1144-1147.

156. Ran, S., Huang, X., Downes, A. and Thorpe, P.E. (2003) Evaluation of novel anti-mouse VEGFR2 antibodies as potential anti-angiogenic or vascular targeting agents for tumor therapy. Neoplasia 5(4), 297-307.

157. Ran S, Mohamedali KA, Luster T, Thorpe P, and Rosenblum MG. (2003) The vascular-ablative agent, VEGF121/rGel, inhibits pulmonary metastases of MDA-MB-231 breast tumors. Neoplasia 5, 297-307.

158. Thorpe, P.E. (2004) Vascular targeting agents as cancer therapeutics. Clin Cancer Res. 10(2):415-427.

159. Cantara S, Donnini S, Giochetti A, Thorpe PE, Ziche M. (2004) Exogenous BH4/Bcl-2 peptide reverts coronary endothelial cell apoptosis induced by oxidative stress. J. Vasc. Res.41(2):202-207.

160. W. Pickering, E. Gray, A. H. Goodall, S. Ran, P. E. Thorpe and T. W. Barrowcliffe. (2004) Characterization of the cell-surface procoagulant activity of T-lymphoblastoid cell lines. J. Thromb. Haemost.2(3):459-467.

161. Ebos JML, Bocci G, Man S, Thorpe PE, Hicklin DJ, Zhou D, Jia X, Kerbel RS. (2004) A

naturally occurring soluble form of vascular endothelial growth factor receptor 2 detected in mouse and human plasma. Mol. Cancer Res. 2(6):315-326.

162. Huang X, Bennet M, Thorpe PE. (2004) Anti-tumor effects and lack of side effects in mice of an immunotoxin directed against human and mouse prostate-specific membrane antigen. The Prostate 61:1-11.

163. Castro-Rivera E, Ran S, Thorpe P, Minna JD. (2004) Semaphorin 3B (SEMA3B) induces apoptosis in lung and breast cancer whereas $VEGF_{165}$ antagonizes this effect. Proc. Natl. Acad. Sci. (USA) 101:11432-11437.

164. Stephan S, Datta K, Wang E, Li J, Brekken RA, Parangi S, Thorpe PE and Mukhopadhyay D. (2004) Effect of rapamycin alone and in combination with anti-angiogenesis therapy in an orthotopic model of human pancreatic cancer. Clin. Cancer Res. 10:6993-7000.

165. Ran S, He J, Huang X, Soares M, Scothorn D, and Thorpe PE. (2005) Anti-tumor effects of a monoclonal antibody directed against anionic phospholipids on the surface of tumor blood vessels in mice. Clin. Cancer Res. 11:1551-1562.

166. Huang X, Bennet M., and Thorpe PE. (2005) A monoclonal antibody that binds anionic phospholipids on tumor blood vessels enhances the anti-tumor effect of docetaxel on human breast tumors in mice. Cancer Res. **65**, 4409-4416.

167. Jennewein M, Qaim SM, Hermanne A, Jahn M, Tsyganov E, Seliounine S, Slavine N, Antich PA, Kulkarni PV, Thorpe PE, Mason RP, Rosch F. (2005) A new method for radiochemical separation of arsenic from irradiated germanium oxide. Appl. Rad. Isotopes **63**, 3:343-351.

168. Mohamedali, K., Sweeney, P. Huang, S., Thorpe, P.E. (2005) The vascular targeting fusion toxin VEGF121/rGel inhibits the growth of orthotopic human bladder carcinoma tumors. Neoplasia Press **7**, 10:912-920(9).

169. Beck, A.W., Luster, T.A., Miller, A.F., Holloway, S.E., Conner, C.R., Barnett, C.C., Thorpe, P.E., Fleming, J.B., and Brekken, R.A. (2006) Combination of a monoclonal anti-phosphatidylserine antibody with gemcitabine strongly inhibits the growth and metastasis of orthotopic pancreatic tumors. Int. J. Cancer **118**, 10:2639-2643

170. Tsyganov, E., Anderson, J., Arbique, G., Coustantinesen, A., Jennewein, M., Kulkarni, P.V., Mason R.P., McColl, R.W., Oz, O., Parkey, R.W., Richer, E., Rosch, F., Seliounine, S., Slavine, N., Srivastava, S.C., Thorpe, P.E., Ziucheuko, A.I., Antiche, P.A. UTSW small animal positron emission luager. IEEE Transactious on Nuclear Science accepted (2006)

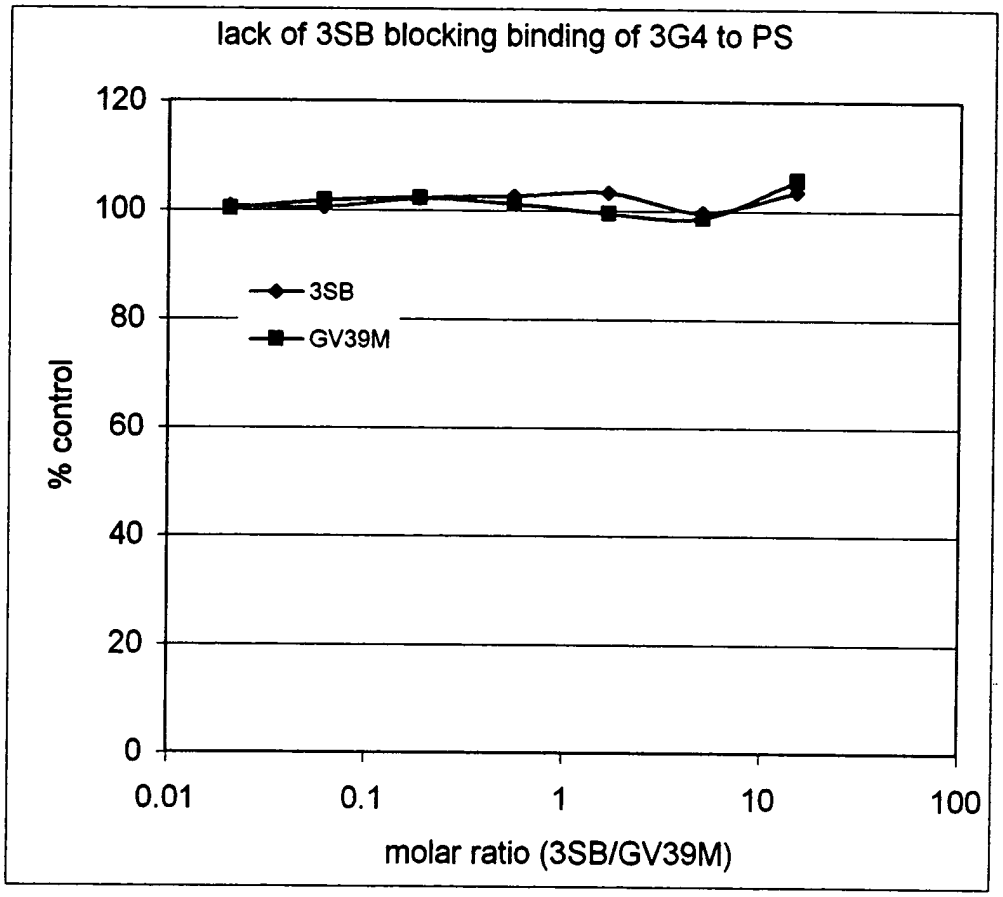
171. Beck, A., Brekken, R., and Thorpe, P.E. Targeting inside-out phospholipids on tumor blood vessels in pancreatic cancer. (Ed. D. Siemann) Kluwer Press (in press)

172. Wilson, J., West, D.C., Thorpe, P.E. Antibody targeting of the tumor vasculature. In "Angiogenesis", Ed., Fan, T.P., Cambridge University Press, UK (in press)

173. Thorpe, P.E., Ran, S. Targeting VCAM-1 and E-selectin on the vessels of solid tumors.

Proceedings of the 26th International Symposium on Controlled Release of Bioactive Materials (in press)

EXHIBIT B


lack of 3SB blocking binding of 3G4 to PS
120
100
80
60
40
20
0
% control
3SB
GV39M
0.01
0.1
1
10
100
molar ratio (3SB/GV39M)